

TABLE 1
 50% INHIBITORY CONCENTRATIONS IC₅₀
 FOR FORMULA A

Example	R ¹	A	mIC50 (μM)	IC50 (μM)	CPP32 IC50 (μM)
4	CH ₃	Ala	0.177	>10	
7	CH ₃	Pro	11.7	>50	
10	CH ₃	Val	0.531	2.48	
13	CH ₃	Leu	5.52	5.62	
16	CH ₃	Phe	3.34	49.8	
21	CH ₃	Gly	34.7	>50	
24	CH ₂ Ph	Ala	0.393	>50	
27	(CH ₂) ₂ CH=CH ₂	Val	0.313	1.45	
30	CH ₂ CO ₂ H	Ala	1.63	>50	
33	(CH ₂) ₂ CO ₂ H	Ala	0.198	>50	
reference	--	--	0.064	47.0	

Fig. 1

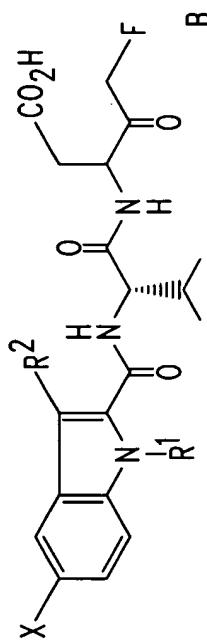


TABLE 2
DISSOCIATION CONSTANT K_i AND INACTIVATION RATE
 k_3/K_i FOR FORMULA B

Example	R ¹	R ²	X	mlCE			CPP32			Mch2			Mch5		
				Ki (μM)	k_3/K_i ($\text{M}^{-1}\text{s}^{-1}$)	k_3/K_i ($\text{M}^{-1}\text{s}^{-1}$)	Ki (μM)	k_3/K_i ($\text{M}^{-1}\text{s}^{-1}$)	k_3/K_i ($\text{M}^{-1}\text{s}^{-1}$)	Ki (μM)	k_3/K_i ($\text{M}^{-1}\text{s}^{-1}$)	k_3/K_i ($\text{M}^{-1}\text{s}^{-1}$)	Ki (μM)	k_3/K_i ($\text{M}^{-1}\text{s}^{-1}$)	
43	CH ₃	CH ₃	H	1.40	2,860	0.960	13,400	0.017	58,800	ND	ND	ND	0.062	21,500	
46	CH ₃	Cl	H	1.68	6,150	0.830	25,900	0.014	71,400	0.054	52,500	0.099	37,000		
49	CH ₃	Cl	F	1.10	7,120	0.493	72,700	0.024	41,700	0.077	32,500	0.054	52,500		
52	(CH ₂) ₃ Ph	H	H	0.133	45,100	0.742	33,700	0.110	74,200	0.036	55,600	0.043	35,300		
55	Ph	H	H	0.843	8,900	0.125	58,700	0.051	19,600	0.038	127,000	0.038	127,000		
58	CH ₂ CO ₂ H	H	H	0.327	16,800	0.240	41,700	0.520	21,200	0.033	30,300	0.026	38,500		
61	CH ₃	H	H	0.397	7,560	0.113	44,200	0.040	25,000	0.102	29,400	0.040	29,400		
62	CH ₃	CH ₃	F	0.327	18,300	0.125	56,000	0.104	19,200	0.038	131,600	0.038	131,600		
63	(CH ₂) ₂ CH=CH ₂	H	H	0.234	21,400	0.180	38,900	0.052	38,500	0.063	47,600	0.063	47,600		
64	CH ₃	CH ₃	H	4.56	1,540	2.28	7,910	0.023	43,500	0.063	31,700	0.063	31,700		
65	CH ₃	CH ₂ CH(CH ₃) ₂	H	0.632	14,200	0.505	21,800	0.038	26,300	0.051	39,200	0.051	39,200		
66	CH ₃	(CH ₂) ₂ Ph	H	0.739	14,900	0.346	31,800	0.040	25,000	0.062	16,100	0.062	16,100		
67	CH ₃	OCH ₂ Ph	--	0.015	278,000	0.820	14,600	0.594	3,370	0.018	83,300	0.018	83,300		
reference	--	--	--	--	--	--	--	--	--	--	--	--	--	--	

Fig. 2

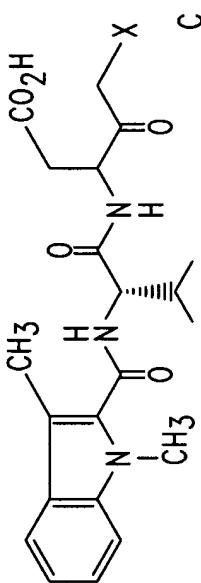


TABLE 3
DISSOCIATION CONSTANT K_i AND INACTIVATION RATE
 k_3/k_1 FOR FORMULA C

Example	X	mlCE		CPP32		Mch2		Mch5	
		K _i (μ M)	k ₃ /K _i (M ⁻¹ s ⁻¹)	K _i (μ M)	k ₃ /K _i (M ⁻¹ s ⁻¹)	K _i (μ M)	k ₃ /K _i (M ⁻¹ s ⁻¹)	K _i (μ M)	k ³ /K _i (M ⁻¹ s ⁻¹)
43	F	1.40	2,860	0.960	13,400	0.017	58,800	0.062	21,500
70	OCO (2, 6-di-Cl-C ₆ H ₃)	1.16	3,460	0.052	57,700	0.030	33,300	0.364	2,750
71	OP(O(C ₆ H ₅) ₂)	0.124	24,200	0.046	65,200	0.060	50,000	0.022	45,500
72	O (1-Ph-3-CF ₃ -pyrazol-5-yl)	0.873	1,150	0.300	16,700	0.050	20,000	1.39	720
73	O (3-CO NH ₂ -2-naphthyl)	8.00	250	1.58	0	0.632	1,580	0.213	0
74	O (2-CO NH ₂ -1-phenyl)	0.297	3,370	0.419	4,770	0.340	2,940	0.547	0
75	OP(O(CH ₃) ₂)	4.33	1,850	1.05	7,660	ND	ND	0.663	1,510
reference	--	0.015	278,00	0.820	14,600	0.594	3,370	0.018	83,300

Fig. 3

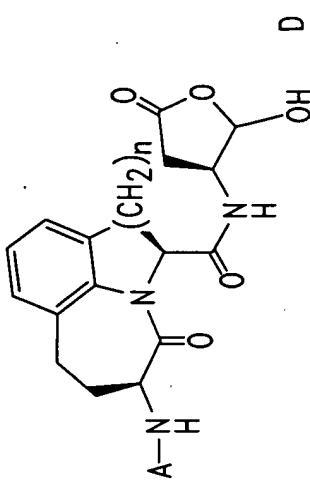
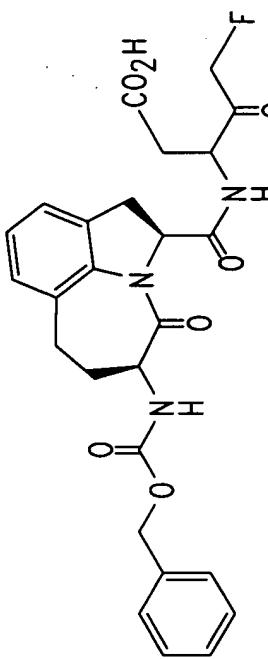


TABLE 4
 50% INHIBITORY CONCENTRATIONS IC₅₀
 FOR FORMULA D

Example No.	A	n	mICE IC ₅₀ (μM)	CPP32 IC ₅₀ (μM)	MCH-2 IC ₅₀ (μM)	MCH-3 IC ₅₀ (μM)	MCH-5 IC ₅₀ (μM)
78	Cbz	1	0.019	1.03	40.1	6.96	>10
82	Ac-Asp	1	0.694	0.0014	6.47	0.145	2.09
85	succinyl	1	0.571	0.245	1.81	2.83	7.98
88	Cbz-Asp	1	0.096	0.00052	ND	0.084	1.19
91	dihydrocinnamoyl	1	0.045	0.780	>10	32.6	18.7
94	Ac	1	3.07	3.87	>10	>50	>50
100	Benzoyl	1	0.159	8.77	>50	>50	4.63
97	1-Naphthoyl	1	0.010	2.91	>50	12.3	1.09
103	Cbz	2	0.026	0.437	32.0	1.11	2.06
reference	-	-	0.064	47.0	>10	>10	2.96

Fig. 4



Example 106

Enzyme	Example 106		<u>Reference</u>
	K _i (μM)	k ₃ /K _i (M ⁻¹ s ⁻¹)	
mICE	0.0005	12,000,000	0.015
CPP32	0.012	960,000	0.820
MCH-2	0.033	25,000	0.594
MCH-5	0.022	98,000	0.018

Fig. 5

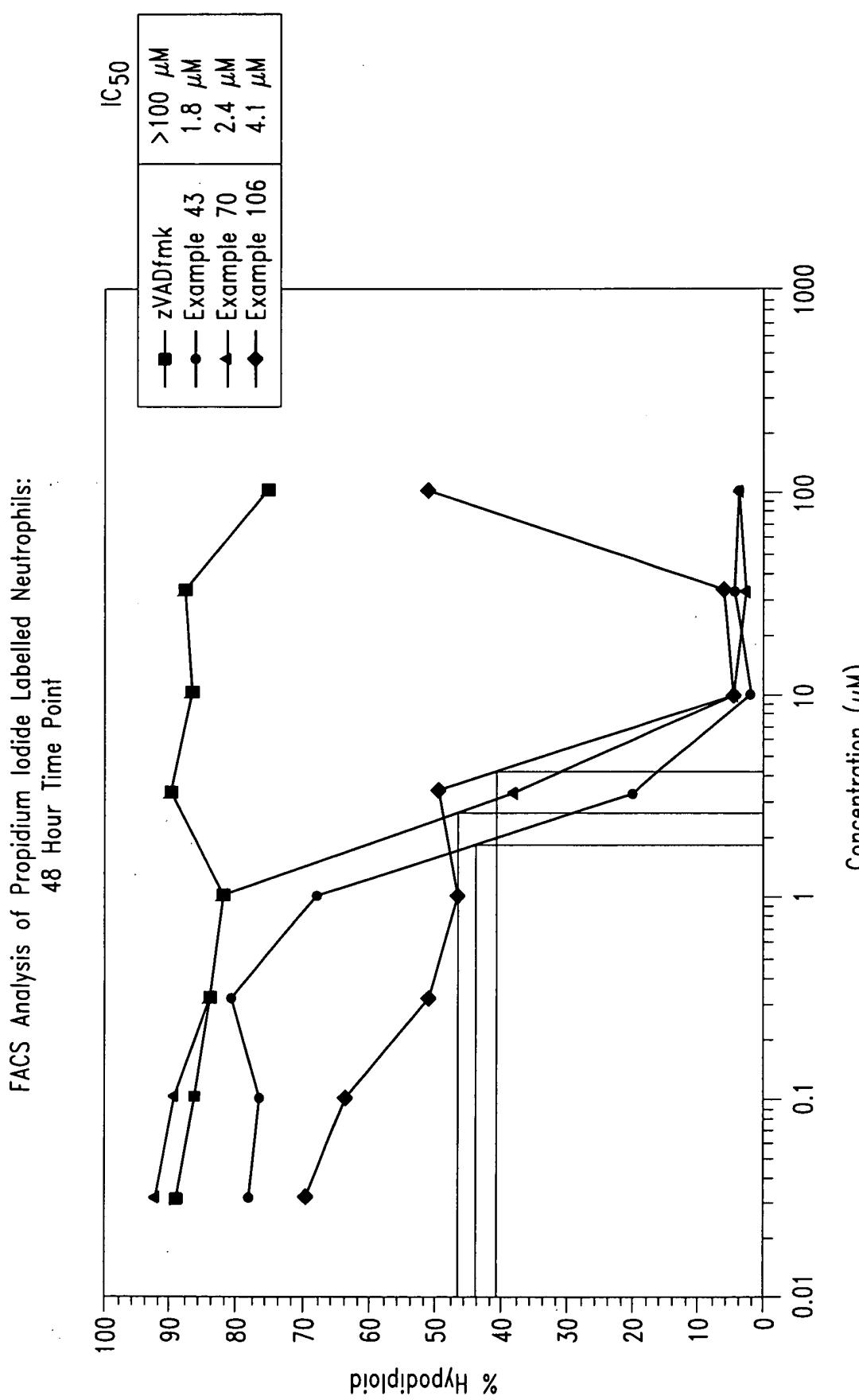


Fig. 6

Neutrophil Survival and Burst Assay

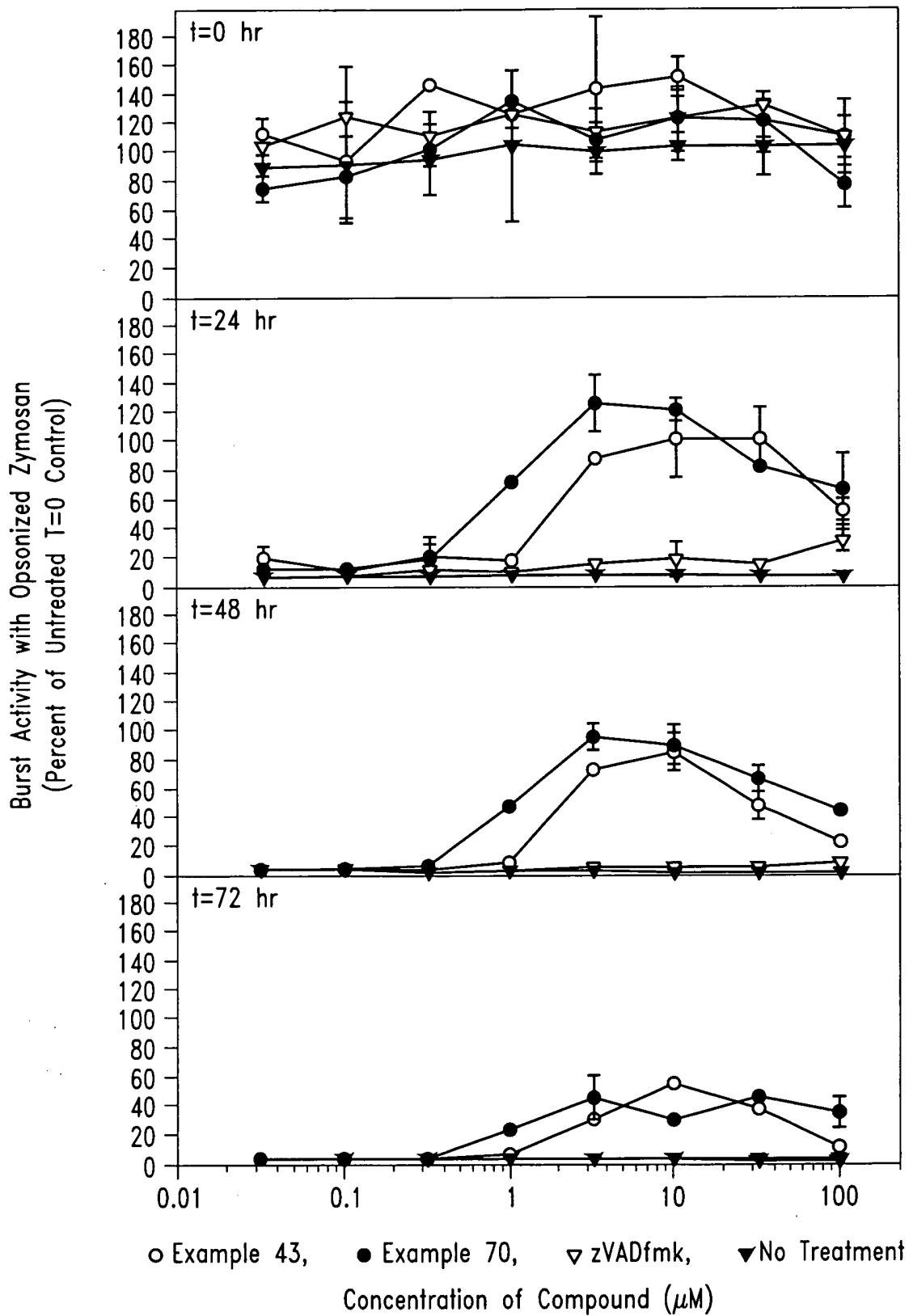


Fig. 7